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May 11, 2015

Delivered via EDGAR

Securities and Exchange Commission
Division of Corporation Finance
100 First Street, N.E.
Mail Stop 4720
Washington, DC 20549

Attn: Daniel Greenspan, Assistant Director

Re: Vertex Pharmaceuticals Incorporated
Form 10-K for the Fiscal Year Ended December 31, 2014
Filed February 13, 2015
File No. 000-19319

Ladies and Gentlemen:

The purpose of this letter is to respond to a comment from the staff (the "Staff") of the Securities and Exchange Commission (the "Commission") to Vertex Pharmaceuticals Incorporated (the "Company") set forth in the Staff's letter to Jeffrey M. Leiden, dated April 28, 2015 (the "Comment Letter"), regarding the Company's Form 10-K for the fiscal year ended December 31, 2014. The comment from the Comment Letter is reproduced below together with the Company's response to the comment.

Business
Collaborations, page 7-8

Comment 1

We note your disclosure regarding your 2014 collaboration agreements with BioAxone Biosciences, Inc. and Janssen Pharmaceuticals, Inc. These agreements appear material to your business. Accordingly, please file each of these agreements as exhibits to your annual report as required under Item 601(b)(10) of Regulation S-K.

Response 1

The Company's business is focused on discovering, developing, manufacturing and commercializing small molecule drugs, primarily related to the treatment of cystic fibrosis. The Company's lead product is KALYDECO®, which accounted for $464 million in net product revenues in 2014, and the Company is seeking approval for a second product, ORKAMBI™, which, if approved, would be used to treat a different, and larger group of patients with cystic fibrosis. In addition, the Company is evaluating a third drug candidate for the treatment of cystic fibrosis in late-stage clinical trials. Accordingly, the Company expects that over the next several years it will derive substantially all of its revenues from its cystic fibrosis products. The Company also maintains a substantial investment in its research and development efforts and its annual operating expenses are in excess of $1.0 billion.

Consistent with other companies in the biopharmaceutical industry, the Company enters into collaboration agreements in the ordinary course of its business (i) to acquire rights to technologies and/or development-stage assets and (ii) to outlicense drug candidates to third-party collaborators. The Company analyzes each collaboration agreement it enters into for materiality when it enters into the agreement and periodically thereafter. For example, the Company has determined that its collaboration agreement with the Cystic Fibrosis Foundation Therapeutics Incorporated is material and currently files it as an exhibit pursuant to Item 601(b)(10) of Regulation S-K. The Company also filed agreements with its collaborators in the field of HCV infection for a number of years pursuant to Item 601(b)(10) of Regulation S-K until the Company decided to exit the HCV infection field and these agreements, therefore, ceased to be material to the Company's business.

Item 601(b)(10)(ii) of Regulation S-K clarifies that if an agreement is such as ordinarily accompanies the kind of business conducted by the registrant, it will be deemed to be made in the ordinary course of business, and therefore not required to be filed, unless the agreement is, one "upon which the registrant's business is substantially dependent." The Company assessed the materiality of the agreements with each of BioAxone Biosciences, Inc. ("BioAxone") and Janssen Pharmaceuticals, Inc. ("Janssen") under this framework and determined, as described below, that (i) each agreement was made in the ordinary course of the Company's business and (ii) the Company's business is not substantially dependent on either of these agreements. Accordingly, the Company did not file these agreements as exhibits to its Annual Report on Form 10-K for the period ended December 31, 2014.

Agreement with Janssen Pharmaceuticals, Inc.

The Company's collaboration agreement with Janssen (the "Janssen Agreement") provides for the grant by the Company to Janssen of a license to develop and commercialize VX-787 (and certain related compounds) for the treatment of influenza ("flu") virus infection. The flu compounds were outlicensed in connection with the Company's decision to exit the field of anti-viral therapies (including the withdrawal from the market of INCIVEK, the Company's product for HCV infection), and the Company's business is not reliant on the Janssen Agreement from an operational or financial perspective.

The Company's primary obligation under the Janssen Agreement is to coordinate an ongoing Phase 2 clinical trial that is funded by Janssen. In 2014, approximately 5 FTEs (out of the Company's approximately 1,800 employees) coordinated the conduct of this clinical trial through a clinical research organization and the Company believes that the number of FTEs on this program will decrease in future periods. The Company's other obligations under the Janssen Agreement (for example, to transfer technical data and maintain certain patents) are not individually or in the aggregate material to the Company. Consistent with the minimal effect that the Janssen Agreement has on the Company's operations, the Company expects no revenues pursuant to the Janssen Agreement in 2015 and net expenses related to the Janssen Agreement of less than $2.0 million in 2015.

Agreement with BioAxone Biosciences, Inc.

The collaboration agreement with BioAxone (the "BioAxone Agreement") provides for a license from BioAxone to the Company to pursue the development VX-210, which the Company is planning to evaluate as a potential treatment for spinal injuries. The BioAxone Agreement represented a small investment by the Company in an early-stage asset in a disease area other than its core focus area of cystic fibrosis.

The Company made a payment of $10.0 million in connection with executing the BioAxone Agreement (representing less than 0.8% of the Company's $1.39 billion in cash, cash equivalents and marketable securities as of December 31, 2014). The Company's only near-term obligation is to conduct a Phase 2

clinical trial, which the Company does not expect to commence until later this year. The BioAxone Agreement did not have a material effect on the Company's operating expenses in 2014 and the Company does not expect it to have a material effect on its operating expenses in 2015 or in future periods.

The Company respectfully submits that neither the Janssen Agreement nor the BioAxone Agreement is material to its business, and requests that the Company be permitted to continue to exclude these agreements from the agreements the Company files pursuant to Item 601(b)(10) of Regulation S-K. Notwithstanding the Company's determination that the agreements are not material under Item 601(b)(10) of Regulation S-K, the Company included disclosure about the agreements in its Form 10-K because it believes it provides meaningful information for investors regarding the Company's third-party collaboration efforts. The Company hereby confirms that, in connection with future filings, it will continue to periodically evaluate its agreements with third parties (including the Janssen Agreement and the BioAxone Agreement) and will file pursuant to Item 601(b)(10) each agreement that it determines as of the date of the relevant filing is material to the Company's business.

The Company acknowledges that:

1) the Company is responsible for the adequacy and accuracy of the disclosure in its filings;

2) Staff comments or changes to disclosure in response to Staff comments do not foreclose the Commission from taking any action with respect to its filings; and

3) the Company may not assert Staff comments as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Please contact me at (617) 961-7018 or Omar White at (617) 341-6396 if you have any questions or concerns with respect to this matter.

Very truly yours,

/s/ Michael J. LaCascia

Michael J. LaCascia
Vice President and Interim General Counsel